Remarks

Amendments to the Claims

Claims 67, 69, 73, 77, 79, and 81 are amended to correct their dependencies. The amendments do not add new matter.

Rejection Under 35 U.S.C. § 112 ¶ 1 (written description)

The Final Office Action maintains the rejection of claims 1, 3, 9, 11, 22, 24, 39, 40, 42, and 58-66 under 35 U.S.C. § 112 ¶ 1 as insufficiently described. Applicants respectfully traverse the rejection.

On page 5, lines 5-8, the Examiner restates the assertion that those skilled in the art would interpret the recitation "hepsin gene" as including genes encoding hepsin subfamily members, including those identified in Appendix 1 to Applicants' previous response (*i.e.*, TMPRSS2, TMPRSS3, TMPRSS4, spinesin, enteropeptidase, and MSPL). The Examiner contends that the specification's disclosure on page 21, lines 12-19 supports this unreasonably broad construction of the recitation "hepsin gene." It does not. The disclosure on page 21, lines 12-19 is reproduced below:

> The term "hepsin" refers to hepsin nucleic acid (DNA and RNA), protein (or polypeptide), and can include their polymorphic variants, alleles, mutants, and interspecies homologs that have (i) substantial nucleotide sequence homology with the nucleotide sequence of the GenBank entry M18930 (human hepsin mRNA, complete cds); or (ii) at least 65% sequence homology with the amino acid sequence of the SWISS-PROT record P05981 (serine protease hepsin); or (iii) substantial nucleotide sequence homology with the nucleotide sequence as set forth in SEQ ID NO: 1; or (iv) substantial sequence homology with the encoded amino acid sequence.

First, the specification plainly states that the term "hepsin" **can** (*i.e.*, does not necessarily) include polymorphic variants, alleles, mutants, and interspecies homologs that meet certain criteria set forth in items (i) through (iv).

Second, using human coding sequences as examples, the sequences encoding the hepsin family members TMPRSS2, TMPRSS3, TMPRSS4, spinesin, enteropeptidase, and MSPL (also known as TMPRSS13) do not have "substantial nucleotide sequence homology with the nucleotide sequence of the GenBank entry M18930 (human hepsin mRNA, complete cds)" as required by item (i) or with SEQ ID NO:1 as required by item (iii). See the BLAST alignments in Appendix 1, which demonstrate in each case "no significant similarity" with GenBank entry M18930.[1] See the BLAST alignment in Appendix 2, which demonstrates that SEQ ID NO:1 and GenBank entry M18930 are identical. In fact, the only sequences which have significant similarity with GenBank entry M18930 are hepsin sequences. See the BLAST results in Appendix 3.

Third, using the human proteins as examples, none of the hepsin subfamily members identified in Appendix 1 to the response filed December 6, 2007 is more than 42% identical to hepsin. Thus, none of these hepsin subfamily members has "at least 65% sequence homology with the amino acid sequence of SWISS-PROT record P05981" (human hepsin) as required by item (ii) or with the amino acid encoded by SEQ ID NO:1 (identical to GenBank entry M18930) as required by item (iv).

There is no evidence of record to support the Examiner's broad construction of the term "hepsin gene." Please withdraw the rejection.

[1] The human enteropeptidase coding sequence available from GenBank is a partial sequence.

Rejection Under 35 U.S.C. § 112 ¶ 1 (enablement)

Claims 1, 3, 9, 11, 22, 24, 40, 42, 44, 45, 52, 58-64, 67-70, 74, and 77-82 stand rejected under 35 U.S.C. § 112 ¶ 1 as not enabled. Applicants respectfully traverse the rejection.

The Examiner contends the specification does not clearly define amplification" (Final Office Action at page 6, lines 4-5) and does not teach analysis of control tissue (Final Office Action at page 7, lines 14-16). On page 8, lines 10-11, the Final Office Action states that it "does not appear that the examples presented in the specification contain proper controls (e.g. non-tumor tissue)." Example 1 ("Amplification of the Hepsin DNA in Tumors and Tumor Cell Lines"), beginning on page 64, explicitly teaches use of a control (emphasis added):

> The genomic DNAs were isolated from ovarian cancer, prostate cancer, breast cancer, and lung cancer cell lines. They were subjected, along with the same hepsin TaqMan probe set as described *supra* representing the target, ***and a reference probe representing a normal non-amplified, single copy region in the genome***, to analysis by TaqMan 7700 Sequence Detector following the manufacturer's protocol.

All of the methods for determining gene amplification known in the art, including those taught in the specification, have inherent detection limits and sensitivities (see, for example, page 65, lines 9-13). For this reason, one skilled in the art could not determine whether the hepsin gene were amplified without comparison to a proper control. In fact, on page 42, lines 20-21, the specification teaches: "Comparison to appropriate controls provides a measure of the copy number of the hepsin gene . . . ."

The specification need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Use of a proper control is not something which needs to be described in detail to enable the claimed methods.

The Examiner has not met her burden to establish a reasonable basis to question the specification's enabling teachings. *In re Wright*, 999 F.2d at 1562, 27 U.S.P.Q.2d at 1513. See also M.P.E.P. § 2164.04. The evidence of record weighs in favor of enablement.

Please withdraw the rejection.

Respectfully submitted,

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